

10/758241

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STRUCTURE FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8
DICTIONARY FILE UPDATES: 17 MAR 2008 HIGHEST RN 1008496-49-8

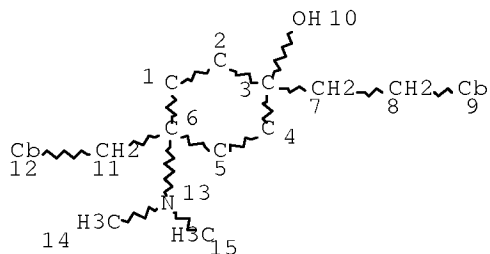
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L1 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
L2 14 SEA FILE=REGISTRY SSS FUL L1

100.0% PROCESSED 624 ITERATIONS 14 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 10:59:13 ON 18 MAR 2008
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FILE COVERS 1907 - 18 Mar 2008 VOL 148 ISS 12
FILE LAST UPDATED: 17 Mar 2008 (20080317/ED)

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They are available for your review at:

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L3 1 L2

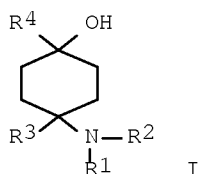
L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:76742 CAPLUS Full-text
DOCUMENT NUMBER: 138:137023
TITLE: Preparation of 4-amino-4-(arylalkyl)cyclohexanols
as ORL1 receptor ligands for treatment of pain
INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich;
Koegel, Babette-yvonne; Wnendt, Stephan
PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|------------------|----------|
| WO 2003008371 | A1 | 20030130 | WO 2002-EP7849 | 20020715 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10135635 | A1 | 20030206 | DE 2001-10135635 | 20010717 |
| DE 10135637 | A1 | 20030206 | DE 2001-10135637 | 20010717 |
| CA 2453843 | A1 | 20030130 | CA 2002-2453843 | 20020715 |
| AU 2002328894 | A1 | 20030303 | AU 2002-328894 | 20020715 |
| AU 2002328894 | B2 | 20070614 | | |
| EP 1406859 | A1 | 20040414 | EP 2002-764691 | 20020715 |
| EP 1406859 | B1 | 20080102 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002011223 | A | 20040810 | BR 2002-11223 | 20020715 |
| HU 2004000207 | A2 | 20040830 | HU 2004-207 | 20020715 |
| CN 1555355 | A | 20041215 | CN 2002-817915 | 20020715 |
| JP 2005504742 | T | 20050217 | JP 2003-513932 | 20020715 |
| NZ 531112 | A | 20050930 | NZ 2002-531112 | 20020715 |
| AT 382601 | T | 20080115 | AT 2002-764691 | 20020715 |

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| | | | | |
|------------------------|----|----------|------------------|------------|
| RU 2315750 | C2 | 20080127 | RU 2004-104628 | 20020715 |
| MX 2004PA00272 | A | 20040504 | MX 2004-PA272 | 20040109 |
| NO 2004000162 | A | 20040311 | NO 2004-162 | 20040114 |
| US 2004214822 | A1 | 20041028 | US 2004-758241 | 20040116 |
| ZA 2004001223 | A | 20041130 | ZA 2004-1223 | 20040216 |
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| | | | DE 2001-10135637 | A 20010717 |
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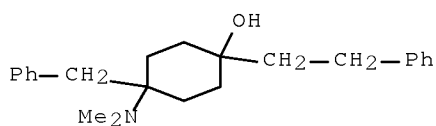
OTHER SOURCE(S): MARPAT 138:137023
GI



AB Title compds. I [wherein R1 and R2 = independently H or (un)substituted (cyclo)alkyl; or NR1R2 = morpholinyl, (un)substituted piperazinyl, pyrrolidinyl, piperidinyl, etc.; R3 = (cyclo)alkyl optionally substituted with cycloalkyl or (hetero)aryl; R4 = (un)substituted cycloalkyl or (hetero)aryl; and racemates, stereoisomers, pharmaceutically acceptable salts, and hydrates thereof] were prepared for treating various indications, especially pain. For example, reaction of 1,4-dioxaspiro[4.5]decan-8-one with dimethylamine•HCl and KCN gave 3-dimethylamino-1,4- dioxaspiro[4.5]decane-8-nitrile. Substitution with benzylmagnesium chloride, conversion to the cyclohexanone, addition of phenethylmagnesium chloride, and recrystn. afforded 4-benzyl-4-dimethylamino-1- phenethylcyclohexanol•HCl. The latter exhibited binding to the ORL1 opioid receptor with Ki of 0.02 μM and demonstrated analgesic activity in the mouse tail flick test with ED50 of 0.015 mg/kg i.v.

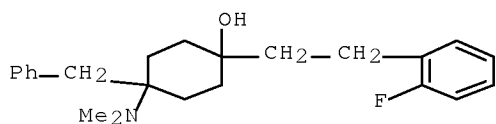
IT 492461-58-2P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol
492461-64-0P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol 492461-66-2P,
4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol
492461-70-8P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol 492461-74-2P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol 492461-78-6P,
4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)

RN 492461-58-2 CAPLUS
CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-
(CA INDEX NAME)



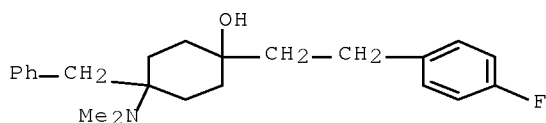
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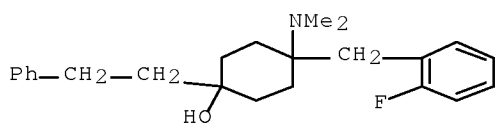
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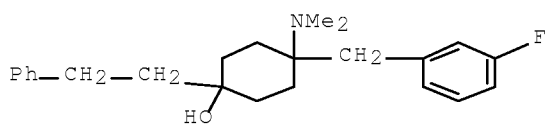
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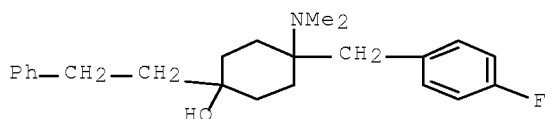
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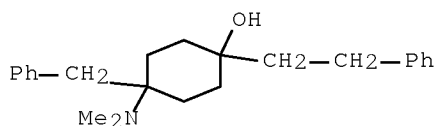


RN 492461-78-6 CAPLUS

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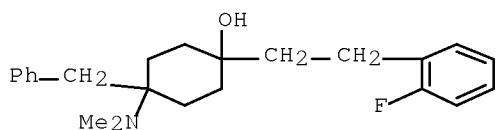


- IT 492461-57-1P, 4-Benzyl-4-dimethylamino-1-phenethylcyclohexanol hydrochloride 492461-63-9P, 4-Benzyl-4-dimethylamino-1-[2-(2-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-65-1P, 4-Benzyl-4-dimethylamino-1-[2-(4-fluorophenyl)ethyl]cyclohexanol hydrochloride 492461-67-3P, 4-Dimethylamino-4-(2-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-71-9P, 4-Dimethylamino-4-(3-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492461-75-3P, 4-Dimethylamino-4-(4-fluorobenzyl)-1-phenethylcyclohexanol hydrochloride 492462-25-6P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol 492462-26-7P, 4-Benzyl-4-dimethylamino-1-[2-(3-fluorophenyl)ethyl]cyclohexanol hydrochloride
- RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (analgesic; preparation of (amino)(arylalkyl)cyclohexanol analgesics starting from dioxaspiro[4.5]decanones, amines, and arylalkylmagnesium chlorides)
- RN 492461-57-1 CAPLUS
- CN Cyclohexanol, 4-(dimethylamino)-1-(2-phenylethyl)-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

- RN 492461-63-9 CAPLUS
- CN Cyclohexanol, 4-(dimethylamino)-1-[2-(2-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)

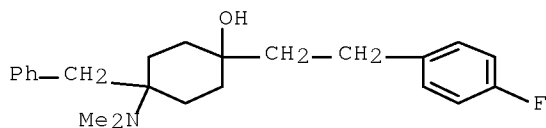


● HCl

- RN 492461-65-1 CAPLUS

10/758241

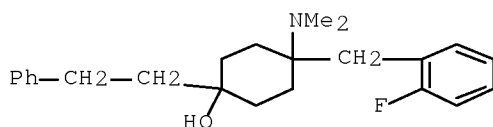
CN Cyclohexanol, 4-(dimethylamino)-1-[2-(4-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-67-3 CAPLUS

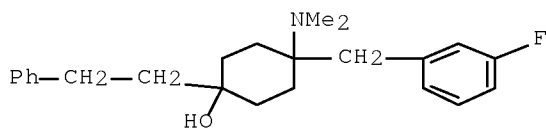
CN Cyclohexanol, 4-(dimethylamino)-4-[(2-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-71-9 CAPLUS

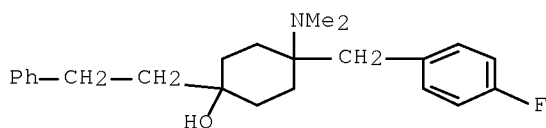
CN Cyclohexanol, 4-(dimethylamino)-4-[(3-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 492461-75-3 CAPLUS

CN Cyclohexanol, 4-(dimethylamino)-4-[(4-fluorophenyl)methyl]-1-(2-phenylethyl)-, hydrochloride (9CI) (CA INDEX NAME)

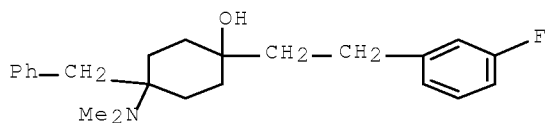


● HCl

10/758241

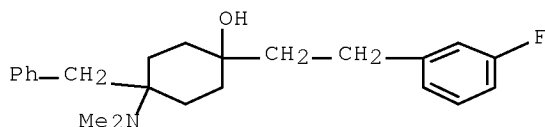
RN 492462-25-6 CAPLUS

CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)- (CA INDEX NAME)



RN 492462-26-7 CAPLUS

CN Cyclohexanol, 4-(dimethylamino)-1-[2-(3-fluorophenyl)ethyl]-4-(phenylmethyl)-, hydrochloride (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L4 0 L2

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L5 0 L2

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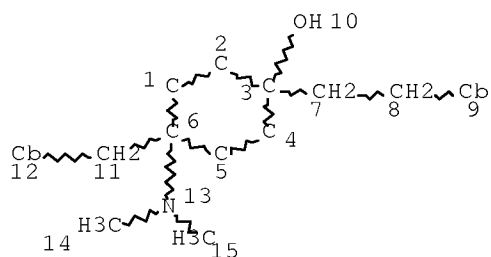
FILE CONTENT: 1961-PRESENT VOL 148 ISS 11 (20080314/ED)
 SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987
 MOST RECENT CITATIONS FOR PATENTS FROM MAJOR ISSUING AGENCIES
 (COVERAGE TO THESE DATES IS NOT COMPLETE):

US 2008027098 31 JAN 2008
 DE 102006031752 10 JAN 2008
 EP 1881549 23 JAN 2008
 JP 2008021517 31 JAN 2008
 WO 2008021152 21 FEB 2008
 GB 2439172 19 DEC 2007
 FR 2903984 25 JAN 2008
 RU 2315659 27 JAN 2008
 CA 2593150 06 JAN 2008

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 have increased from 100,000 to 200,000 for both on-line and batch
 searches. For more information on MARPAT search limits, type HELP
 SLIMITS at an arrow prompt.

L6 STR



NODE ATTRIBUTES:
 DEFAULT MLEVEL IS ATOM
 MLEVEL IS CLASS AT 9 12
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
 RING(S) ARE ISOLATED OR EMBEDDED
 NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
 ECLEVEL IS LIM ON ALL NODES

10/758241

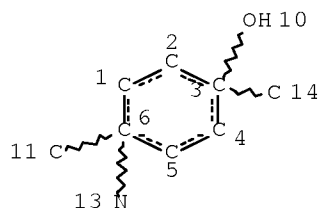
ALL RING(S) ARE ISOLATED

L8 0 SEA FILE=MARPAT SSS FUL L6 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 49148 ITERATIONS
SEARCH TIME: 00.00.22

0 ANSWERS

L9 STR



NODE ATTRIBUTES:

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NSPEC IS RC AT 13
NSPEC IS RC AT 14
CONNECT IS X2 RC AT 1
CONNECT IS X2 RC AT 2
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CONNECT IS X2 RC AT 5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 10

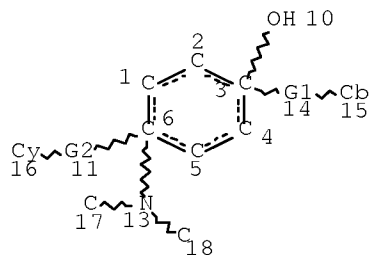
STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L10 (212) SEA FILE=MARPAT SSS FUL L9 (MODIFIED ATTRIBUTES)

L11 STR



REP G1=(0-2) CH2
REP G2=(0-1) CH2
NODE ATTRIBUTES:

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 MLEVEL IS CLASS AT 15 16
 DEFAULT ECLEVEL IS LIMITED

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 NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
 ECLEVEL IS LIM ON ALL NODES
 ALL RING(S) ARE ISOLATED

L12 7 SEA FILE=MARPAT SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)

100.0% PROCESSED 162 ITERATIONS 7 ANSWERS
 SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 11:11:17 ON 18 MAR 2008
 L13 7 S L12
 L14 6 S L13 NOT L3

FILE 'MARPAT' ENTERED AT 11:11:36 ON 18 MAR 2008
 L15 6 S L14

L15 ANSWER 1 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 147:357143 MARPAT Full-text
 TITLE: Thioredoxin and thioredoxin reductase inhibitors
 INVENTOR(S): Schaus, Scott E.; Eastwood, Erin L.
 PATENT ASSIGNEE(S): Trustees of Boston University, USA
 SOURCE: PCT Int. Appl., 89pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2007103273 | A2 | 20070913 | WO 2007-US5530 | 20070302 |
| WO 2007103273 | A3 | 20071122 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA,
 CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
 GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE,
 KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA,
 MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG,
 PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY,
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
 IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,
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 ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: US 2006-778876P 20060303

AB The present invention relates to sulfone derivs. and to their use as modulators of the thioredoxin/thioredoxin reductase redox system, including for the treatment and/or prevention of pathophysiol. conditions mediated by thioredoxin/thioredoxin reductase, such as cancer, HIV/ AIDS, Alzheimer's disease, rheumatoid arthritis, and skin disorders. Also provided are pharmaceutical compns. comprising the inventive sulfones. The targets of a novel tetrazole-containing compound, 4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)butanenitrile (PTSB) that inhibited cell growth of A549 lung carcinoma cells, were determined by studying the changes in steady-state gene expression in *Saccharomyces cerevisiae* upon treatment with PTSB using oligonucleotide arrays, the MNI algorithm, and the reverse-engineered network model. Two genes, for thioredoxin reductase and for thioredoxin were identified and then confirmed by a biochem. assay. A library of 36 compds. was designed and developed to include the sulfone and/or the nitrile functionalities and tested in a cancer cell growth inhibition assay.

L15 ANSWER 2 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 146:168880 MARPAT Full-text
 TITLE: Wrinkle-preventive/ameliorating agents comprising
 α -amino acid derivatives
 INVENTOR(S): Tsunenaga, Makoto; Iwaki, Haruhi; Iida, Toshii;
 Kaminuma, Mikiko; Suetsugu, Masaru; Takada, Keiko;
 Inomata, Shinji
 PATENT ASSIGNEE(S): Shiseido Company, Ltd., Japan
 SOURCE: PCT Int. Appl., 53pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|------------------|----------|
| WO 2007013662 | A1 | 20070201 | WO 2006-JP315248 | 20060726 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

PRIORITY APPLN. INFO.: JP 2005-215426 20050726

AB Disclosed is a wrinkle-preventive/ameliorating agent comprising one or more compds. selected from the group consisting of an α -amino acid derivative represented by the general formula, NR₁R₂CHR₁C(:O)OR₄ and a salt thereof, wherein R₁ represents H, CH₃ or CH₂OH; R₂ and R₃ independently represent H, C₁-4-alkyl group, or R₂ and R₃, together with N atom may form a C₄-6 cyclic structure which may have O; and R₄ represents H, C₁-18 alkyl, provided that a situation where one of R₂ and R₃ is a benzyloxycarbonyl group and the other is H does not occur when both R₁ and R₄ represent H. For example, antiwrinkle cream contained sarcosine 20, stearic acid 5, stearyl alc. 4, iso-Pr myristate 18, glycerin monostearate 3, propylene glycol 10, KOH 0.2, preservatives q.s., perfumes q.s., and ion-exchanged water balance to 100 %.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR

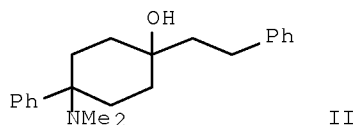
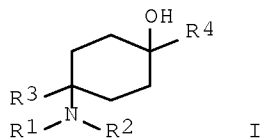
10/758241

THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L15 ANSWER 3 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 138:136953 MARPAT Full-text
 TITLE: Preparation of substituted 4-aminocyclohexanols as
 regulators for the nociceptin/orphanin FQ ligand
 ORL-1 receptor system
 INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-heinrich;
 Englberger, Werner; Wnendt, Stephan
 PATENT ASSIGNEE(S): Gruenenthal Gmbh, Germany
 SOURCE: PCT Int. Appl., 133 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|------------------|----------|
| WO 2003008370 | A1 | 20030130 | WO 2002-EP7842 | 20020715 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10135636 | A1 | 20030206 | DE 2001-10135636 | 20010717 |
| CA 2453901 | A1 | 20030130 | CA 2002-2453901 | 20020715 |
| AU 2002321215 | A1 | 20030303 | AU 2002-321215 | 20020715 |
| AU 2002321215 | B2 | 20070802 | | |
| EP 1406858 | A1 | 20040414 | EP 2002-754882 | 20020715 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| HU 2004001082 | A2 | 20040830 | HU 2004-1082 | 20020715 |
| JP 2004534858 | T | 20041118 | JP 2003-513931 | 20020715 |
| MX 2004PA00446 | A | 20040318 | MX 2004-PA446 | 20040115 |
| US 2004236104 | A1 | 20041125 | US 2004-758242 | 20040116 |
| US 7183436 | B2 | 20070227 | | |
| PRIORITY APPLN. INFO.: | | | DE 2001-10135636 | 20010717 |
| | | | WO 2002-EP7842 | 20020715 |

GI



AB Title compds. I [R1-2 = H, alkyl, cycloalkyl, etc.; R3 = (hetero)aryl; R4 = cycloalkyl, (hetero)aryl, etc.] are prepared For instance, 1,4-dioxaspiro[4.5]decan-8-one was converted to 8-dimethylamino-1,4-

dioxaspiro[4.5]decan-8-carbonitrile (MeOH, Me₂NH, KCN). Displacement of this intermediate with phenylmagnesium chloride followed by deprotection and subsequent treatment with phenethylmagnesium chloride results in the formation of II. II has K_i = 4.4 nM for the ORL-1 receptor. I are useful for treating pain.

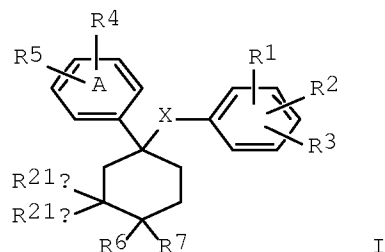
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L15 ANSWER 4 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

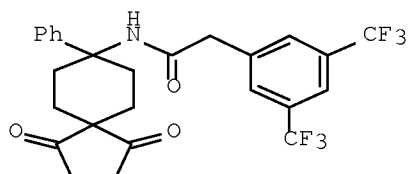
ACCESSION NUMBER: 136:5907 MARPAT Full-text
TITLE: Synthesis of aryl-amido-cyclohexane derivatives
and their use as NK-1 receptor antagonists
INVENTOR(S): Castro Pineiro, Jose Luis; Dinnell, Kevin;
Elliott, Jason Matthew; Hollingworth, Gregory
John; Shaw, Duncan Edward; Swain, Christopher John
PATENT ASSIGNEE(S): Merck Sharp & Dohme Limited, UK
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2001087838 | A1 | 20011122 | WO 2001-GB2145 | 20010516 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2408849 | A1 | 20011122 | CA 2001-2408849 | 20010516 |
| EP 1286967 | A1 | 20030305 | EP 2001-929829 | 20010516 |
| EP 1286967 | B1 | 20060927 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2003533509 | T | 20031111 | JP 2001-584234 | 20010516 |
| AT 340781 | T | 20061015 | AT 2001-929829 | 20010516 |
| ES 2273837 | T3 | 20070516 | ES 2001-929829 | 20010516 |
| US 2003236250 | A1 | 20031225 | US 2002-276127 | 20021113 |
| US 7105507 | B2 | 20060912 | | |
| PRIORITY APPLN. INFO.: | | | GB 2000-12240 | 20000519 |
| | | | WO 2001-GB2145 | 20010516 |

GI



I



II

AB Title compds. I [ring A = Ph or pyridyl; X = linker selected from amido(carbonyl), amino, ester, ether; R1 = OH, (fluoro)alkyl, alkenyl, cycloalkyl, (fluoro)alkoxy, etc.; R2 = H, halo, alkyl, alkoxy or R1-2 with the atom to which they are attached, may form a 5 - 6 membered ring; R3 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, cycloalkyl, CN, etc. or R3 = 5 - 6 membered heterocyclic ring; R4 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, OH, NO2, CN, etc.; R5 = H, halo, (fluoro)alkyl, alkoxy; R6 = H, OH, alkyl; R7 = H, OH, alkylamino, alkylcarboxy, carbocyclyl, C-linked heterocyclyl or heteroaryl or R6-7 together represent :O, :CH-ester, ketal; R21a = H, halo, OH; R21b = H, or R21a-21b = F or together represent :O] were prepared Over 300 synthetic examples were disclosed. For instance, 3,5- bis(trifluoromethyl)benzeneacetic acid was converted to the acid chloride derivative (CH2Cl2, ClCOCOC1, DMF, room temperature, 1 h), and used to acylate 1,4-dioxo-8-phenylspiro[4.5]decan-8-amine (preparation given, dichloroethane, Et3N, room temperature) to give II as a brown gum in quant. yield. I are neurokinin 1 (NK-1) receptor antagonists (no data). Compds. I are of particular use in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 6 MARPAT COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 124:260852 MARPAT Full-text
 TITLE: Improved Chichibabin aminations of pyridine bases
 INVENTOR(S): Lawin, Phillip B.; Sherman, Angela R.; Grendze, Martin P.
 PATENT ASSIGNEE(S): Reilly Industries, Inc., USA
 SOURCE: PCT Int. Appl., 44 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| WO 9600216 | A1 | 19960104 | WO 1995-US8030 | 19950626 |

10/758241

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, DE, EE, FI, GE, HU, IS,
JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ,
PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE,
IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML,
MR, NE, SN, TD, TG

| | | | | |
|------------|----|----------|-----------------|----------|
| IL 114314 | A | 20001206 | IL 1995-114314 | 19950625 |
| CA 2193236 | A1 | 19960104 | CA 1995-2193236 | 19950626 |
| AU 9529100 | A | 19960119 | AU 1995-29100 | 19950626 |
| AU 703530 | B2 | 19990325 | | |
| EP 766675 | A1 | 19970409 | EP 1995-924694 | 19950626 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,
PT, SE

| | | | | |
|-------------|----|----------|----------------|----------|
| BR 9508123 | A | 19970812 | BR 1995-8123 | 19950626 |
| CN 1156990 | A | 19970813 | CN 1995-194733 | 19950626 |
| HU 76424 | A2 | 19970828 | HU 1996-3557 | 19950626 |
| HU 217172 | B | 19991228 | | |
| JP 10502089 | T | 19980224 | JP 1996-503374 | 19950626 |
| RU 2165414 | C2 | 20010420 | RU 1997-101086 | 19950626 |
| IN 183814 | A1 | 20000429 | IN 1995-CA744 | 19950630 |
| US 5808081 | A | 19980915 | US 1996-765281 | 19961220 |

PRIORITY APPLN. INFO.:

| | |
|----------------|----------|
| US 1994-265321 | 19940624 |
| US 1995-480440 | 19950607 |
| WO 1995-US8030 | 19950626 |

OTHER SOURCE(S): CASREACT 124:260852

AB Improved Chichibabin aminations of pyridine bases are described which are conducted under a pressurized gas phase containing ammonia and in the presence of a selected additive [e.g., R1X(CH2)nXR2 wherein X = S, O, NR3, CO2; R1 - R3 = H, alkyl, etc.; n = 0 - 12] which increases the reaction rate, and also in preferred processes favorably alters the isomer ratios and product yields from the aminations while benefiting product workup and recovery as well. Thus, amination of pyridine in toluene containing NaNH2 and monoethanolamine gave 2-aminopyridine. The use of monoethanolamine greatly reduces the reaction time.

L15 ANSWER 6 OF 6 MARPAT COPYRIGHT 2008 ACS on STN

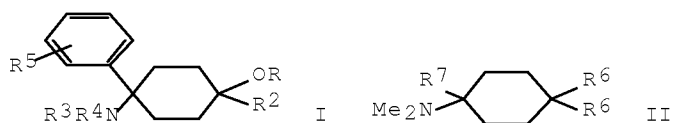
ACCESSION NUMBER: 91:74328 MARPAT Full-text
TITLE: 4-Aminocyclohexanols, their acylates and acid
addition salts
INVENTOR(S): Lednicer, Daniel
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: Ger. Offen., 58 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| ----- | ---- | ----- | ----- | ----- |
| DE 2839891 | A1 | 19790412 | DE 1978-2839891 | 19780913 |
| US 4366172 | A | 19821228 | US 1977-837510 | 19770929 |
| GB 2005266 | A | 19790419 | GB 1978-38272 | 19780927 |
| GB 2005266 | B | 19820203 | | |
| FR 2404625 | A1 | 19790427 | FR 1978-27780 | 19780928 |
| FR 2404625 | B1 | 19811224 | | |
| JP 54059263 | A | 19790512 | JP 1978-120333 | 19780929 |
| CH 635818 | A5 | 19830429 | CH 1978-10157 | 19780929 |

PRIORITY APPLN. INFO.:

| | |
|----------------|----------|
| US 1977-837510 | 19770929 |
|----------------|----------|

GI



AB Aminocyclohexanols I [R = H, R1CO (R1 = C1-3 alkyl); R2 = H, C1-6 aliphatic group, cycloalkylalkyl (optionally unsatd.), (substituted) phenylalkyl; R3, R4 = C1-5 alkyl; R5 = H, halo, OH, C1-3 alkyl in meta or para position] and their physiol. acceptable salts, useful as analgesics (no data) were prepared Thus, 4-hydroxycyclohexanone was successively acetalized with (HOCH2)2, 4-hydroxycyclohexanone ethylene ketal oxidized with CrO3 (91% yield), 1,4-cyclohexanedione mono(ethylene ketal) cyanated with KCN and aminated with Me2NH.HCl (78% yield), nitrile II (R6R6 = OCH2CH2O, R7 = cyano) treated with 4-ClC6H4MgBr (34% yield), phenylcyclohexanone ketal II (R6R6 = OCH2CH2O, R7 = 4-ClC6H4) hydrolyzed with 2N HCl in MeOH (70% yield), and ketone II (R6R6 = O, R7 = 4-ClC6H4) reduced with NaBH4 to give 30% cyclohexanol I (R = R2 = H, R3 = R4 = Me, R5 = 4-Cl).

FILE 'REGISTRY' ENTERED AT 11:14:53 ON 18 MAR 2008

L17 113 SEA ABB=ON PLU=ON ?BENZYL-4-DIMETHYLAMINO?/CNS
L18 21 SEA ABB=ON PLU=ON L16(L)L17

FILE 'CAPLUS' ENTERED AT 11:15:17 ON 18 MAR 2008

L19 3 SEA ABB=ON PLU=ON L18
L20 35 SEA ABB=ON PLU=ON (4(W)(BENZYL OR BZ))(1W)(DIMETHYLAMINO?
OR DI(W)(METHYLAMINO? OR (ME OR METHYL)(W)AMINO?) OR
DIMETHYL AMINO?)
L21 2 SEA ABB=ON PLU=ON L20(S)(?CYCLOHEXANOL? OR ?CYCLO
HEXANOL?)
L22 2 SEA ABB=ON PLU=ON (L19 OR L21) NOT L3

L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

ED Entered STN: 24 Jan 2008

ACCESSION NUMBER: 2008:94964 CAPLUS Full-text

DOCUMENT NUMBER: 148:191845

TITLE: Preparation of cyclohexylindoles as opioid
receptor-like 1 (ORL1) receptor inhibitors
INVENTOR(S): Zemolka, Saskia; Schunk, Stefan; Englberger,
Werner; Koegel, Babette-Yvonne; Linz, Klaus;
Schick, Hans; Sonnenschein, Helmut; Graubaum,
Heinz; Hinze, Claudia

PATENT ASSIGNEE(S): Gruenenthal GmbH, Germany

SOURCE: PCT Int. Appl., 303pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|----------|-----------------|----------|
| WO 2008009415 | A2 | 20080124 | WO 2007-EP6325 | 20070717 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, | | | | |

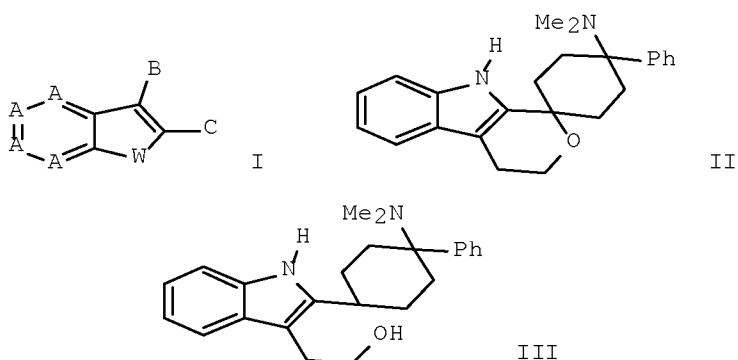
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OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM,
SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA,
ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU,
IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,
ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

DE 102006033109 A1 20080131 DE 2006-102006033109 20060718
PRIORITY APPLN. INFO.: DE 2006-102006033109A 20060718

OTHER SOURCE(S): MARPAT 148:191845
GI



AB Title compds. I [A = N, CR⁷⁻¹⁰; B, C = H, alkyl, cycloalkyl, etc.; R⁷, R⁸, R⁹, R¹⁰ = H, halo, NO₂, etc.; W = O, S, NR₄, preferably NH; R₄ = H, C₁₋₅ alkyl, etc.] and their pharmaceutically acceptable salts and formulations were prepared For example, tin-mediated reduction of pyranose II gave the citrate salt of claimed indole III. In ORL1 receptor inhibition assays, 6 examples of compds. I exhibited K_i values ranging from 0.0009-3 μM.

IT 492462-14-3P 492462-23-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(preparation of cyclohexylindoles as opioid receptor-like 1 (ORL1)
receptor inhibitors)

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN

ED Entered STN: 03 Oct 2003

ACCESSION NUMBER: 2003:777742 CAPLUS Full-text

DOCUMENT NUMBER: 139:291992

TITLE: Preparation of substituted 4-aminocyclohexanols
for treatment of pain

INVENTOR(S): Sundermann, Bernd; Hennies, Hagen-Heinrich;
Englberger, Werner; Koegel, Babette-Yvonne

PATENT ASSIGNEE(S): Gruenenthal G.m.b.H., Germany

SOURCE: PCT Int. Appl., 124 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

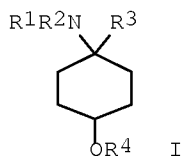
LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2003080557 | A1 | 20031002 | WO 2003-EP2812 | 20030318 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10213051 | A1 | 20031030 | DE 2002-10213051 | 20020323 |
| CA 2480038 | A1 | 20031002 | CA 2003-2480038 | 20030318 |
| AU 2003212366 | A1 | 20031008 | AU 2003-212366 | 20030318 |
| EP 1487778 | A1 | 20041222 | EP 2003-708253 | 20030318 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005526795 | T | 20050908 | JP 2003-578315 | 20030318 |
| US 2005187220 | A1 | 20050825 | US 2004-947551 | 20040923 |
| US 7211694 | B2 | 20070501 | | |
| PRIORITY APPLN. INFO.: | | | DE 2002-10213051 | A 20020323 |
| | | | WO 2003-EP2812 | W 20030318 |

OTHER SOURCE(S): CASREACT 139:291992; MARPAT 139:291992
GI



AB Aminocyclohexanols I [R1, R2 = H, (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R1R2 = CH2CH2OCH2CH2, (un)substituted CH2CH2NHCH2CH2, (CH2)3-6; R3 = (un)substituted aliphatic, cycloalkyl, aryl, heterocyclyl; R4 = (un)substituted cycloalkyl, aryl, heterocyclyl] were prepared. Thus, 1,4-dioxaspiro[4.5]decan-8-one was reduced to the alc., o-benzylated, hydrolyzed to the ketone, and treated with Me2NH>HCl and KCN to give 4-benzyloxy-1-dimethylaminocyclohexanecarbonitrile which was treated with PhMgBr and NH4Cl to give I [R1, R2 = Me, R3 = Ph, R4 = PhCH2] whose diastereomers were separated. The diastereomers had IC50 for ORL-1 binding of 0.069 and 0.40 μM, resp.

IT 607717-22-6P, 4-Benzyl-4-dimethylaminocyclohexanol

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted 4-aminocyclohexanols for treatment of pain)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR

10/758241

THIS RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

FILE 'MEDLINE' ENTERED AT 11:18:33 ON 18 MAR 2008

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L23 1 S L21

L23 ANSWER 1 OF 1 WPIX COPYRIGHT 2008 THE THOMSON CORP on STN
ACCESSION NUMBER: 2003-267985 [26] WPIX
DOC. NO. CPI: C2003-069839 [26]
TITLE: New substituted 4-aminocyclohexanol derivatives, are
ORL1 receptor ligands useful e.g. for treating
anxiety, depression, epilepsy, Alzheimer's disease,
cardiovascular disease or especially pain
DERWENT CLASS: B05
INVENTOR: HENNIES H; HENNIES H H; KOEGEL B; KOEGEL B Y; KOEGEL
B; SUNDERMANN B; WNENDT S
PATENT ASSIGNEE: (CHEF-C) GRUENENTHAL GMBH
COUNTRY COUNT: 99

PATENT INFO ABBR.:

| PATENT NO | KIND | DATE | WEEK | LA | PG | MAIN IPC |
|----------------|------|----------|-----------|----|-----|----------|
| WO 2003008371 | A1 | 20030130 | (200326)* | DE | 75 | [0] |
| DE 10135635 | A1 | 20030206 | (200326) | DE | | |
| DE 10135637 | A1 | 20030206 | (200326) | DE | | |
| EP 1406859 | A1 | 20040414 | (200426) | DE | | |
| KR 2004029369 | A | 20040406 | (200451) | KO | | |
| AU 2002328894 | A1 | 20030303 | (200452) | EN | | |
| BR 2002011223 | A | 20040810 | (200455) | PT | | |
| HU 2004000207 | A2 | 20040830 | (200465) | HU | | |
| US 20040214822 | A1 | 20041028 | (200471) | EN | | |
| MX 2004000272 | A1 | 20040501 | (200482) | ES | | |
| JP 2005504742 | W | 20050217 | (200513) | JA | 115 | |
| CN 1555355 | A | 20041215 | (200519) | ZH | | |
| ZA 2004001223 | A | 20050223 | (200519) | EN | 104 | |
| NO 2004000162 | A | 20040311 | (200557) | NO | | |

10/758241

| | | | | |
|---------------|----|----------|----------|----|
| NZ 531112 | A | 20050930 | (200566) | EN |
| AU 2002328894 | B2 | 20070614 | (200765) | EN |
| EP 1406859 | B1 | 20080102 | (200805) | DE |
| RU 2315750 | C2 | 20080127 | (200810) | RU |
| DE 50211466 | G | 20080214 | (200813) | DE |

APPLICATION DETAILS:

| PATENT NO | KIND | APPLICATION | DATE |
|----------------|------------|------------------|----------|
| WO 2003008371 | A1 | WO 2002-EP7849 | 20020715 |
| DE 10135635 | A1 | DE 2001-10135635 | 20010717 |
| DE 10135637 | A1 | DE 2001-10135637 | 20010717 |
| AU 2002328894 | A1 | AU 2002-328894 | 20020715 |
| AU 2002328894 | B2 | AU 2002-328894 | 20020715 |
| BR 2002011223 | A | BR 2002-11223 | 20020715 |
| CN 1555355 | A | CN 2002-817915 | 20020715 |
| EP 1406859 | A1 | EP 2002-764691 | 20020715 |
| EP 1406859 | B1 | EP 2002-764691 | 20020715 |
| NZ 531112 | A | NZ 2002-531112 | 20020715 |
| EP 1406859 | A1 | WO 2002-EP7849 | 20020715 |
| BR 2002011223 | A | WO 2002-EP7849 | 20020715 |
| HU 2004000207 | A2 | WO 2002-EP7849 | 20020715 |
| US 20040214822 | A1 Cont of | WO 2002-EP7849 | 20020715 |
| MX 2004000272 | A1 | WO 2002-EP7849 | 20020715 |
| JP 2005504742 | W | WO 2002-EP7849 | 20020715 |
| NO 2004000162 | A | WO 2002-EP7849 | 20020715 |
| NZ 531112 | A | WO 2002-EP7849 | 20020715 |
| EP 1406859 | B1 | WO 2002-EP7849 | 20020715 |
| RU 2315750 | C2 | WO 2002-EP7849 | 20020715 |
| JP 2005504742 | W | JP 2003-513932 | 20020715 |
| HU 2004000207 | A2 | HU 2004-207 | 20020715 |
| RU 2315750 | C2 | RU 2004-104628 | 20020715 |
| MX 2004000272 | A1 | MX 2004-272 | 20040109 |
| NO 2004000162 | A | NO 2004-162 | 20040114 |
| KR 2004029369 | A | KR 2004-700679 | 20040116 |
| US 20040214822 | A1 | US 2004-758241 | 20040116 |
| ZA 2004001223 | A | ZA 2004-1223 | 20040216 |
| DE 50211466 | G | DE 2002-50211466 | 20020715 |
| DE 50211466 | G | EP 2002-764691 | 20020715 |
| DE 50211466 | G | WO 2002-EP7849 | 20020715 |

FILING DETAILS:

| PATENT NO | KIND | PATENT NO |
|---------------|-------------|-----------------|
| EP 1406859 | A1 Based on | WO 2003008371 A |
| AU 2002328894 | A1 Based on | WO 2003008371 A |
| BR 2002011223 | A Based on | WO 2003008371 A |
| HU 2004000207 | A2 Based on | WO 2003008371 A |
| MX 2004000272 | A1 Based on | WO 2003008371 A |
| JP 2005504742 | W Based on | WO 2003008371 A |
| NZ 531112 | A Based on | WO 2003008371 A |
| AU 2002328894 | B2 Based on | WO 2003008371 A |
| EP 1406859 | B1 Based on | WO 2003008371 A |
| RU 2315750 | C2 Based on | WO 2003008371 A |
| DE 50211466 | G Based on | EP 1406859 A |
| DE 50211466 | G Based on | WO 2003008371 A |

PRIORITY APPLN. INFO: DE 2001-10135635 20010717

DE 2001-10135637 20010717

AN 2003-267985 [26] WPIX

AB WO 2003008371 A1 UPAB: 20060119

NOVELTY - 1,4-Disubstituted 4-aminocyclohexanol derivatives (I) are new.
 DETAILED DESCRIPTION - Aminocyclohexanol derivatives of formula (I) (including racemates and pure stereoisomers (specifically enantiomers or diastereomers) or their mixtures) and their salts (specifically hydrochlorides) and solvates (specifically hydrates) are new.

R1, R2, R5 = H, alkyl or cycloalkyl (both optionally unsaturated and optionally substituted), Ar or -Q-Cyc; or NR1R2 = morpholino, 4-(R5)-piperazino, azetidino, pyrrolidino, piperidino or homopiperidino;

Ar = aryl or heteroaryl (both optionally substituted); Q = 1-3C alkylene;

Cyc = optionally substituted cycloalkyl or Ar; R3 = alkyl or cycloalkyl (both optionally unsaturated and optionally substituted), Ar or -Q'-Cyc; Q' = optionally unsaturated, optionally substituted 1-4C alkylene;

R4 = Cyc, -CHR6(CH2)nR7, -C(Y)(CH2)nR7 or -R8-L-R9; n = 0-3;

Y = O, S or H2;

R6 = H, or 1-7C alkyl or 1-6C alkoxy carbonyl (both optionally unsaturated and optionally substituted); R7 = H or Cyc;

R8 = Ar;

L = CONH, NHCO, COO, OCO, O, S or SO2; and R9 = Ar;

provided that: alkyl moieties have 1-8C and cycloalkyl moieties 3-8C unless specified otherwise; and R1 and R2 are not both H. An INDEPENDENT CLAIM is also included for the preparation of (I).

ACTIVITY - Analgesic; Tranquilizer; Antidepressant; Anticonvulsant; Neuroprotective; Nootropic; Antiaddictive; Antialcoholic; Vasotropic; Cardiant; Hypotensive; Hypertensive; Auditory; Antipruritic; Antimigraine; Anorectic; Antidiarrheic; Immunomodulator; Uropathic; Relaxant; Antitussive; Anesthetic; Diuretic; Antidiuretic.

In a mouse tail-flick test for analgesic activity, 4-benzyl-4-dimethylamino-1-phenethyl-cyclohexanol (Ia) hydrochloride displayed an ED50 of 0.015 mg/kg when administered intravenously.

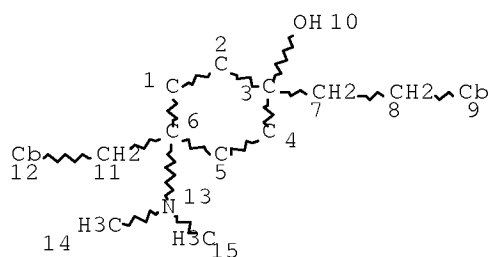
MECHANISM OF ACTION - Opioid-Like Receptor 1 Ligand (ORL1); nociceptin/ORL1 Receptor Modulator. In an ORL1 receptor binding assay, 4-benzyl-4-dimethylamino-1-phenethyl-cyclohexanol (Ia) hydrochloride displayed a Ki of 0.02 microM.

USE - (I) Are used: for treatment of pain (especially acute, visceral, neuropathic or chronic pain); for treatment of anxiety states, stress and associated syndromes, depression, epilepsy, Alzheimer's disease, senile dementia, general cognitive dysfunction, learning and memory difficulties, withdrawal symptoms, alcohol, drug or medicament abuse or dependence, sexual dysfunction, cardiovascular disease, hypotension, hypertension, tinnitus, pruritis, migraine, hearing deficiency, gastric motility deficiency, eating disorders, anorexia, obesity, locomotor disorders, diarrhea, cachexia or urinary incontinence; as nootropic agents, muscle relaxants, anticonvulsants, antitussive agents or anesthetics; for coadministration with other opioid analgesics or with anesthetics; or for diuresis, antinatriuresis and/or anxiolysis (all claimed). (I) Are especially useful for treating pain.

ADVANTAGE - (I) Have high affinity for the ORL1 receptor and low toxicity.

FILE 'HOME' ENTERED AT 11:20:17 ON 18 MAR 2008

L1 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

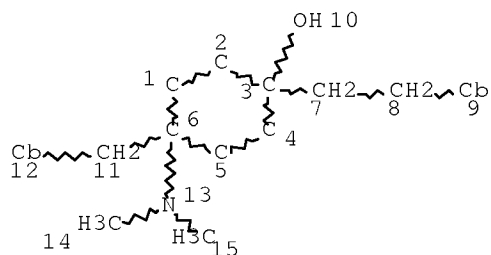
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NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

L2 14 SEA FILE=REGISTRY SSS FUL L1

L6 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 9 12

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

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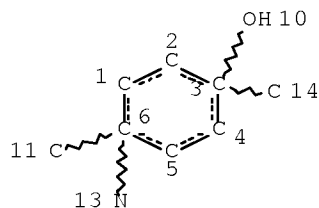
ECLEVEL IS LIM ON ALL NODES

ALL RING(S) ARE ISOLATED

L7 0 SEA FILE=MARPAT SSS SAM L6 (MODIFIED ATTRIBUTES)

L9

STR



NODE ATTRIBUTES:

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NSPEC   IS RC      AT   13
NSPEC   IS RC      AT   14
CONNECT IS X2   RC AT    1
CONNECT IS X2   RC AT    2
CONNECT IS X2   RC AT    4
CONNECT IS X2   RC AT    5
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS   10

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STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:

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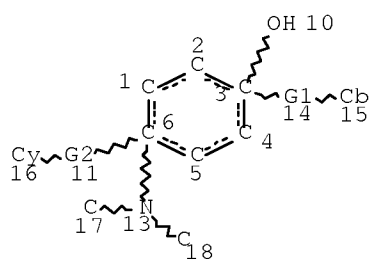
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

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L10 (      212)SEA FILE=MARPAT SSS FUL L9 (MODIFIED ATTRIBUTES)
L11          STR

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REP G1=(0-2) CH2

REP G2=(0-1) CH2

NODE ATTRIBUTES:

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NSPEC   IS RC      AT   13
CONNECT IS X2   RC AT    1
CONNECT IS X2   RC AT    2
CONNECT IS X2   RC AT    4
CONNECT IS X2   RC AT    5
DEFAULT MLEVEL IS ATOM
MLEVEL   IS CLASS  AT  15 16
DEFAULT ECLEVEL IS LIMITED

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GRAPH ATTRIBUTES:

10/758241

RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L12 7 SEA FILE=MARPAT SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)

(FILE 'REGISTRY' ENTERED AT 10:58:22 ON 18 MAR 2008)
ACT BROOK758/A

L1 STR
L2 14 SEA SSS FUL L1

D QUE STAT

FILE 'CAPLUS' ENTERED AT 10:59:13 ON 18 MAR 2008
L3 1 SEA ABB=ON PLU=ON L2
D IBIB ABS HITSTR

FILE 'CAOLD' ENTERED AT 10:59:31 ON 18 MAR 2008
L4 0 SEA ABB=ON PLU=ON L2

FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 10:59:38 ON 18 MAR 2008
L5 0 SEA ABB=ON PLU=ON L2

FILE 'MARPAT' ENTERED AT 10:59:42 ON 18 MAR 2008
L6 STR L1
L7 0 SEA SSS SAM L6 (MODIFIED ATTRIBUTES)
L8 0 SEA SSS FUL L6 (MODIFIED ATTRIBUTES)
ACT BROOKM/A

L9 STR
L10 (212)SEA SSS FUL L9 (MODIFIED ATTRIBUTES)
L11 STR
L12 7 SEA SUB=L10 SSS FUL L11 (MODIFIED ATTRIBUTES)

D QUE STAT L8
D QUE STAT L12

FILE 'CAPLUS' ENTERED AT 11:11:17 ON 18 MAR 2008
L13 7 SEA ABB=ON PLU=ON L12
L14 6 SEA ABB=ON PLU=ON L13 NOT L3

FILE 'MARPAT' ENTERED AT 11:11:36 ON 18 MAR 2008
L15 6 SEA ABB=ON PLU=ON L14
D 1-6

FILE 'REGISTRY' ENTERED AT 11:12:24 ON 18 MAR 2008
L16 31479 SEA ABB=ON PLU=ON ?CYCLOHEXANOL?/CNS
L17 113 SEA ABB=ON PLU=ON ?BENZYL-4-DIMETHYLAMINO?/CNS
L18 21 SEA ABB=ON PLU=ON L16(L)L17

FILE 'CAPLUS' ENTERED AT 11:15:17 ON 18 MAR 2008
L19 3 SEA ABB=ON PLU=ON L18
L20 35 SEA ABB=ON PLU=ON (4(W)(BENZYL OR BZ))(1W)(DIMETHYLAMINO?
OR DI(W)(METHYLAMINO? OR (ME OR METHYL)(W)AMINO?) OR

10/758241

DIMETHYL AMINO?)
L21 2 SEA ABB=ON PLU=ON L20(S) (?CYCLOHEXANOL? OR ?CYCLO
HEXANOL?)
L22 2 SEA ABB=ON PLU=ON (L19 OR L21) NOT L3
D 1-2

FILE 'MEDLINE, BIOSIS, EMBASE, WPIX, JAPIO, PASCAL, DISSABS' ENTERED
AT 11:18:33 ON 18 MAR 2008

L23 1 SEA ABB=ON PLU=ON L21
D IBIB ABS

FILE 'HOME' ENTERED AT 11:20:17 ON 18 MAR 2008

D QUE L2
D QUE L7
D QUE L12

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FILE CAOLD
FILE COVERS 1907-1966

10/758241

FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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FILE MEDLINE

FILE LAST UPDATED: 15 Mar 2008 (20080315/UP). FILE COVERS 1949 TO DA

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FILE BIOSIS

FILE COVERS 1926 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT FROM JANUARY 1926 TO DATE.

RECORDS LAST ADDED: 12 March 2008 (20080312/ED)

BIOSIS has been augmented with 1.8 million archival records from 1926 through 1968. These records have been re-indexed to match current BIOSIS indexing.

FILE EMBASE

FILE COVERS 1974 TO 18 Mar 2008 (20080318/ED)

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FILE MARPAT

FILE CONTENT: 1961-PRESENT VOL 148 ISS 11 (20080314/ED)

SOME MARPAT RECORDS ARE DERIVED FROM INPI DATA FOR 1961-1987

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US 2008027098 31 JAN 2008

10/758241

DE 102006031752 10 JAN 2008
EP 1881549 23 JAN 2008
JP 2008021517 31 JAN 2008
WO 2008021152 21 FEB 2008
GB 2439172 19 DEC 2007
FR 2903984 25 JAN 2008
RU 2315659 27 JAN 2008
CA 2593150 06 JAN 2008

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FILE WPIX

FILE LAST UPDATED: 13 MAR 2008 <20080313/UP>
MOST RECENT THOMSON SCIENTIFIC UPDATE: 200818 <200818/DW>
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>>> IPC Reform backfile reclassification has been loaded to the end of November 2007. No update date (UP) has been created for the reclassified documents, but they can be identified by 20060101/UPIC and 20061231/UPIC, 20070601/UPIC, 20071001/UPIC and 20071130/UPIC. <<<

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http://www.stn-international.de/stndatabases/details/ico_0801.zip

http://www.stn-international.de/stndatabases/details/epc_0801.zip

Supplement of all changed ECLA items:

http://www.stn-international.de/stndatabases/details/ecla_0802s.zi

FILE JAPIO

FILE LAST UPDATED: 3 MAR 2008 <20080303/UP>

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FILE PASCAL

FILE LAST UPDATED: 17 MAR 2008 <20080317/UP>

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